CHAPTER 5

Anxiety

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Studies have shown that 14.6% to 15.6% of patients in primary care settings have anxiety disorders. These patients do not typically identify themselves as having "anxiety." Many of these patients initially present with nonspecific somatic complaints, and they tend to exhibit high health care use; 50% of patients with diagnosed anxiety disorders receive treatment services for these symptoms in primary care settings. Anxiety disorders can significantly impair individuals' ability to function in daily routines, so they are at risk for financial problems, interpersonal problems, poor health habits, academic decline, and work productivity problems. Anxiety disorders often elicit cardiopulmonary, GI, genitourinary, and neurologic symptoms. Anxiety disorders have even been shown to exacerbate coronary artery disease and increase cardiovascular mortality rate. It is important to recognize that certain medical conditions and chemicals can cause symptoms of anxiety (see "Secondary Causes of Anxiety"). These secondary or organic causes of anxiety should be addressed primarily.

Anxiety disorders include:

- Generalized anxiety disorder
- Panic disorder
- Agoraphobia
- Social phobias
- Specific phobias
- Obsessive-compulsive disorder
- Posttraumatic stress disorder
- Acute stress disorder
- Separation anxiety disorder
- Anxiety disorder due to a general medical condition
- Substance-induced anxiety disorder
- Anxiety disorder not otherwise specified (typically mixed anxiety-depression)

Adjustment disorder with anxiety can temporarily mimic some of these clinical anxiety disorders.

Epidemiology data (Table 5-1) for anxiety disorders show a strong familial pattern, yet it is apparent that both genetic and environmental factors play a role in anxiety disorders.

Table 5-1. Epidemiology of Common Anxiety Disorders

	LIFETIME PREVALENCE	GENDER DIFFERENCE	AGE OF ONSET	TYPICAL FAMILIAL PATTERN	GENERAL COURSE
Generalized anxiety disorder (GAD)	5%	F > M	20s	Yes	Fluctuating/chronic
Obsessive-compulsive disorder (OCD)	1% to 2.5%	F = M	Childhood to early adult	Yes	Episodic/potentially chronic
Panic disorder (PD)	1% to 3.5%	F > M	18-35	Yes	Episodic/potentially chronic
Posttraumatic stress disorder (PTSD)	8%	F = M	Any	Yes	Variable/potentially chronic
Separation anxiety disorder (SEP)	4%	F ≥ M	Childhood	Yes	Episodic/situational
Social phobia (SOP)	3% to 13%	F ≥ M	Mid-teens	Yes	Continuous/chronic
Specific phobia (SPP)	7.2% to 11.3%	F ≥ M	Childhood or mid-20s	Yes	Episodic/situational

GENERALIZED ANXIETY DISORDER

Generalized anxiety disorder (GAD) is characterized by excessive apprehension and uncontrollable worry about multiple events or activities. The focus of the worry often shifts from one area of concern to another. Children and adolescents tend to focus more on performance issues, while adults will worry more about routine life circumstances. These symptoms can be distressing, and they interfere with the patient's quality of life or daily functioning. The anxiety is not confined to the features of another psychiatric disorder, medical condition, or the physiologic effects of a substance. Although a minimum of 6 months of anxiety symptoms is necessary for diagnosis, many patients have experienced these symptoms for years prior to seeking treatment.

GAD has a high comorbidity rate with depression, panic disorder, social phobia, specific phobias, somatization disorders, substance abuse, and personality disorders. GAD also has a high co-occurrence with hyperthyroidism, chronic fatigue syndrome, fibromyalgia, diabetes, irritable bowel syndrome, peptic ulcer disease, tension headaches, hypertension, ischemic stroke, chronic obstructive pulmonary disease (COPD), and heart disease. Some electroencephalogram (EEG) abnormalities are common with GAD (e.g., alpha rhythm and evoked potentials), and EEG sleep discontinuity includes a decrease in stage 1, delta, and rapid eye movement (REM) sleep.

Symptoms

- Excessive anxiety ++++
- Uncontrollable worry ++++
- Irritability ++++
- Restlessness ++++
- Muscle tension +++
- Concentration problems +++
- Sleep problems (typically insomnia) +++
- Stomachache or nausea +++
- Shortness of breath ++
- Palpitations ++
- Headache ++
- Fatigue ++

Signs

- Cognitive vigilance +++
- Excessive sweating +++
- Diarrhea +

Workup

- Medical examination for differential diagnosis: Review medical history. Endocrine system problems, brain tumors, toxin exposure, stimulant intoxication, and withdrawal (e.g., from alcohol, benzodiazepines, sedatives) can present symptoms of GAD.

- Thyroid function tests (TSH, T_4) are generally recommended. A basic metabolic panel (BMP) and an ECG may also be warranted (see "Secondary Causes of Anxiety").
- Clinical interview: Include mental status examination current psychosocial stressors; family (genetic) history of substance abuse, medical, or psychiatric disorders; and patient history of psychiatric, medical, or substance abuse problems or treatment services.
- Differential diagnosis or comorbidity screening indicated for other anxiety disorders, mood disorders, adjustment disorders, somatoform disorders, personality disorders, factitious disorders, eating disorders, psychosis, and suicidal ideations
- Structured diagnostic interviews and instruments: Primary Care Evaluation of Mental Health Disorders (PRIME-MD), Mini-International Neuropsychiatric Interview (MINI), Symptom Driven Diagnostic System for Primary Care (SDDS-PC), Structured Clinical Interview for DSM-IV (SCID), and Quick PsychoDiagnostics (QPD) Panel
- Screening checklists: Generalized Anxiety Disorder Questionnaire (GADQ-IV), Generalized Anxiety Disorder-7 (GAD-7), Beck Anxiety Inventory for Primary Care (BAI-PC), Penn State Worry Questionnaire (PSWQ), and Depression Anxiety Stress Scale (DASS).

Comments and Treatment Considerations

Initiate patient education regarding GAD and discuss treatment options. Consider the high comorbidity of GAD with depression (as well as other psychiatric/ medical conditions) when developing the treatment plan and when selecting psychotropic medications.

Buspirone is effective with GAD (without the risk of dependency, withdrawal, or relapse risks common with benzodiazepines), although it is often not effective with the associated comorbidities of GAD.

Benzodiazepines are primarily useful for acute symptoms of GAD, yet antidepressants are considered to be more effective for long-term symptom management.

SSRIs (escitalopram, paroxetine, and sertraline) and serotonin-norepinephrine reuptake inhibitor (SNRIs) (venlafaxine) antidepressants are approved by the US Food and Drug Administration (FDA) for treatment of GAD. Other SSRI medications are likely to be effective as well due to class effect. Tricyclic antidepressants can be effective with GAD, yet they are not a "front-line" option due to anticholinergic side effects, overdose potential, and cardiovascular risks. The FDA has advised monitoring patients for suicidal ideations after starting antidepressant medications.

Strong evidence-based research supports the effectiveness of cognitive-behavioral therapy (CBT) for GAD. It has shown effectiveness equal to pharmacotherapy. Applied relaxation is another very effective therapeutic technique for GAD. CBT is compatible with pharmacotherapy, and CBT maintains gains beyond medication discontinuation. Collaborative care models of treatment have promise for GAD.

PANIC DISORDER

Panic disorder (PD) is characterized by having unexpected panic attacks and an intense discomfort or fear regarding the possibility of having future panic attacks. It is common for people to worry about the implications of the panic attacks because they may feel that they are having a heart attack, breathing problems, or that they are "going crazy." Panic attacks are defined as an intense and abrupt fear or discomfort with multiple somatic or cognitive symptoms. These symptoms are out of context to the setting (i.e., no emergency is actually taking place). Panic attacks typically peak within 10 minutes and often end within 20 to 60 minutes. Panic attacks tend to occur on a variable frequency rate. During a panic attack the person may fear death, loss of control, or imminent danger.

Nocturnal panic attacks can occur during stage II and stage II sleep. Situationally bound panic attacks may actually stem from a phobia instead of a panic disorder, whereas panic disorder is typically signaled by unexpected panic attacks. Panic attacks have been associated with cerebral vasoconstriction, temporal lobe involvement, and multiple neurotransmitters: norepinephrine (NE), serotonin (5-HT), gamma-aminobutyric acid (GABA), and cholecystokinin tetrapeptide (CCK-4). It is of note that cigarette smokers are up to three times more likely to have panic attacks than nonsmokers.

If patients associate the panic attack with a certain setting or situation they may attempt to avoid certain environments in a quest to prevent panic attacks. They sometimes make major life decisions (such as quitting a job or refusing a promotion that involves travel) to reduce the perceived odds of having a panic attack. They may be especially avoidant of settings and situations in which escape is difficult or help appears difficult to access (e.g., agoraphobia). Not all panic disorders include agoraphobia, and some people have agoraphobia without a history of panic disorder (this is not common). PD has a very high comorbidity with social phobia and specific phobias.

Symptoms

- Panic attacks (recurrent and unexpected) ++++
- Intense fear of having additional panic attacks ++++
- Behavioral changes +++
- Agoraphobia +++
- Nausea +++
- Dizziness +++
- Paresthesias ++
- Concentration problems +

Signs

- Palpitations or chest pain +++
- Autonomic hyperactivity +++
- Depersonalization or derealization +++
- Sweating +++
- Tachycardia +
- Dyspnea +

Workup

- Medical examination for differential diagnosis: Review medical history. Screen for endocrine disorders, cardiovascular disease, respiratory disorders, temporal lobe epilepsy, vestibular disorders, and substance abuse.
- Due to the cardiac symptoms of this disorder, an ECG is often warranted.
- Depending on the patient's presenting symptoms, the utility of a CBC, complete metabolic panel (CMP), TSH, urinalysis, and a drug screen should be considered (see "Secondary Causes of Anxiety").
- Clinical interview: Include mental status examination; current psychosocial stressors; family (genetic) history of substance abuse, medical, or psychiatric disorders; and patient history of psychiatric, medical, or substance abuse problems and treatment services.
- Differential diagnosis or comorbidity screening indicated for other anxiety disorders, mood disorders, somatoform disorders, personality disorders, factitious disorders, eating disorders, psychosis, and suicidal ideations
- Structured diagnostic interview and instruments: Primary Care Evaluation of Mental Health Disorders (PRIME-MD), Mini-International Neuropsychiatric Interview (MINI), Symptom Driven Diagnostic System for Primary Care (SDDS-PC), Structured Clinical Interview for DSM-IV (SCID), and Quick PsychoDiagnostics (QPD) Panel
- Screening checklists: Brief Panic Disorder Screen (BPDS), Panic Disorder Severity Scale (PDSS), NIMH Panic Questionnaire, Panic and Agoraphobia Scale (PAS), Albany Panic and Phobia Questionnaire (APPQ), and Beck Anxiety Inventory for Primary Care (BAI-PC)

Comments and Treatment Considerations

After a diagnosis of panic disorder, a health care provider will need to spend psychoeducational time with the patient. Because of the intensity of the distress and somatic symptoms, it is initially difficult for a patient to believe that the panic attacks stem from an anxiety disorder. Reassurance and supportiveness from a health care provider can go a long way with helping the patient gain acceptance of this diagnosis.

Consider the high comorbidity of PD with social phobia or specific phobias when developing the treatment plan.

Alprazolam can be effective for rapid symptom control, whereas SSRIs are considered to be a more conservative option for long-term symptom management. Both alprazolam and paroxetine have FDA approval for the treatment of panic disorder. Benzodiazepines must be slowly discontinued because abrupt discontinuation can elicit a recurrence of panic attacks.

Tricyclic medications (such as clomipramine and imipramine) can be effective for PD; however, they can be deadly in overdose. Monitor the risks of anticholinergic side effects, overdose potential,

and cardiovascular distress. The FDA has advised monitoring patients for suicidal ideations after starting antidepressant medications.

There is strong evidence-based research supporting the effectiveness of CBT for panic disorder, and these gains appear to be long lasting. Exposure techniques, cognitive strategies, and relaxation techniques have shown effectiveness.

Collaborative care models of treatment have promise for PD because studies have shown that combining psychologic treatments with psychotropic medication improves treatment prognosis. Routine exercise has also been shown to reduce symptoms of PD. A reduction in caffeine and nicotine use is generally advisable.

SECONDARY CAUSES OF ANXIETY

Secondary conditions that cause anxiety symptoms include anxiety disorder due to a general medical condition and substance-induced anxiety disorder. These anxiety disorders cause significant distress and impairment in daily functioning, and they can mimic the symptoms of other anxiety disorders. Neither diagnosis is given if the anxiety symptoms occur only during a delirium or if the anxiety is best accounted for by another psychiatric disorder.

Anxiety disorder due to a general medical condition is diagnosed when the direct physiologic effects of a medical condition have caused clinical anxiety features. Endocrine (e.g., hyperthyroidism, hypoparathyroidism, hypoglycemia, pheochromocytoma), cardiovascular (e.g., cardiac arrhythmia, cardiomyopathy, mitral valve prolapse), respiratory (e.g., asthma, COPD), metabolic (vitamin B_{12} deficiency, porphyria), and neurologic (cerebral neoplasms, encephalitis, etc.) problems can directly produce anxiety. Inflammatory disorders (e.g., lupus erythematosus, rheumatoid arthritis), pregnancy, and perimenopause are also associated with anxiety.

Substance-induced anxiety disorder is diagnosed when the physiologic consequences of a substance have directly caused anxiety symptoms. Toxin exposure, substance intoxication, and substance withdrawal can produce symptoms of various clinical anxiety disorders. Substances that often cause anxiety during intoxication and withdrawal include alcohol, cocaine, amphetamine, cannabis, hallucinogens, inhalants, hypnotics, anxiolytics, sedatives, phencyclidine, nicotine, and caffeine.

Many over-the-counter medications (i.e., decongestants and weight-loss tablets) and prescription drugs (i.e., methylphenidate, narcoleptics, corticosteroids, anticholinergics, β-adrenergic agonists, and SSRIs) have anxiety as a possible side effect. Antianxiety medications (such as benzodiazepines) can actually induce anxiety when discontinued. Toxins that can induce anxiety include mercury, phosphorus, arsenic, benzene, and carbon disulfide, for example. Dioxin and theophylline toxicity can cause anxiety symptoms.

Symptoms
- Panic attacks ++
- Obsessions and compulsions ++
- Generalized anxiety ++
- Agitation +
- Phobias (not common in general medical conditions) +
- Palpitations and chest pain +
- Nausea +
- Dizziness +
- Paresthesias +

Signs
- Cognitive impairments +
- Tachycardia +
- Dyspnea +
- Sweating +
- Autonomic hyperactivity +

Workup
- *Clinical interview:* Include mental status examination; current psychosocial stressors; family (genetic) history of substance abuse, medical, or psychiatric disorders; and patient history of psychiatric, medical, or substance abuse problems and treatment services. Screen for mood disorders, personality disorders, and malingering.
- Differential diagnosis or comorbidity screening indicated for other anxiety disorders, mood disorders, somatoform disorders, personality disorders, factitious disorders, eating disorders, psychosis, and suicidal ideations
- *History:* Etiology of the anxiety symptoms must be shown to be related to the general medical condition or substance exposure. Temporal associations (onset, exacerbation, and remission of symptoms) and atypical symptoms for clinical anxiety disorders provide clues to the secondary causes of the anxiety.
- Consider side effect profiles and interactions between current medications.
- *Structured diagnostic interviews and instruments:* Symptom Driven Diagnostic System for Primary Care (SDDS-PC)
- *Medical examination for differential diagnosis:* Screen for endocrine disorders, cardiovascular disease, respiratory disorders, temporal lobe epilepsy, vestibular disorders, toxin exposure, and substance abuse.
- A CMP, TSH, CBC, ECG, urinalysis, and a drug screen provide important information regarding secondary causes of anxiety. A CMP helps assess for diabetes, liver disease, and kidney disease. The TSH helps to screen for hyper- or hypothyroidism. A CBC can be helpful to screen for anemia, infections, and inflammation. The ECG helps to reveal cardiac problems. Urinalysis helps detect metabolic and kidney disorders. The drug screen detects substance abuse problems (which the patient may not initially disclose).

- Spirometry testing and bronchodilator reversibility testing can be useful to screen for asthma and COPD. Additional studies may necessitate an EEG or vestibular testing.

Comments and Treatment Considerations

A full substance abuse assessment is indicated when it is determined that alcohol, illicit drugs, or prescription drug abuse contributes to the patient's anxiety level. Inpatient substance abuse services, outpatient substance abuse services, Alcoholics Anonymous or Narcotics Anonymous (AA/NA) meetings, or medical detox options may be necessary.

Extended removal of the substance or toxin should result in a reduction in the anxiety level. Encourage a healthy lifestyle (e.g., routine exercise, appropriate diet, good sleep hygiene, no substance abuse). A change in medication may be necessary, if any of the patient's medications have anxiety as a side effect, interaction, or withdrawal effect.

If the patient's medical problems produce anxiety symptoms, treatment of the underlying medical condition should produce a reduction in anxiety symptoms. Further assessment or differential diagnosis is indicated if improvements are not noted with the preceding approaches.

SOCIAL PHOBIA (SOCIAL ANXIETY DISORDER)

Social phobia is characterized by having a significant fear of social or performance situations in which embarrassment or humiliation can occur. It is much more intense and distressing than simply being shy, and the exposure to certain social encounters can immediately elicit a physical anxiety response. Situational panic attacks can occur in social phobia. These patients show functional impairments, avoidant behaviors, anxious anticipation, and a diminished quality of life. Despite such impairments patients are generally reluctant to seek help for social anxiety, and this diagnosis can easily be missed by health care providers.

Adults often identify that this fear is excessive, and they often want to be "normal" socially. Children and teens can display transient social anxiety symptoms without developing social phobia. Early childhood language impairment appears to be a precursor for social phobia. For those younger than 18 years of age, the symptoms must persist for at least 6 months to qualify for the social phobia diagnosis. Many people with social phobia will only display the symptoms in certain situations (such as meeting strangers, dating, or public speaking). Social phobia has a subclassification of "generalized type," which is to be noted if fear occurs in most social interaction or performance situations. This subtype represents about one third of patients with social phobia.

Patients with social phobia are likely to exhibit anticipatory anxiety regarding certain social interactions, perfectionism, and then self-criticism regarding their performance. They may worry that others are aware of their physical symptoms of anxiety (i.e., blushing,

trembling, dry mouth). The diagnosis is not given if the embarrassment is primarily about symptoms of another known medical or psychiatric disorder. Social phobia has a high comorbidity rate with GAD, dysthymic disorder, major depressive disorder, PD, specific phobias, and avoidant personality disorder. It often co-occurs with eating disorders and alcohol abuse.

Symptoms

- Excessive fear (in one or more social interaction/performance situations) +++++
- Embarrassment or humiliation concerns ++++
- Anxiety or anxious anticipation ++++
- Distress +++
- Avoidance +++
- Panic attacks (situational) +
- Palpitations +

Signs

- Impaired social relationships +++
- Blushing ++
- Situational tremors ++
- Sweating +
- Diarrhea +

Workup

- Clinical interview: Include mental status examination; current psychosocial stressors; family (genetic) history of substance abuse, medical, or psychiatric disorders; and patient history of psychiatric, medical, or substance abuse problems and treatment services.
- Differential diagnosis or comorbidity screening indicated for other anxiety disorders, mood disorders, somatoform disorders, personality disorders, factitious disorders, eating disorders, psychosis, and suicidal ideations
- Screening checklists: Liebowitz Social Anxiety Scale (LSAS), Social Phobia Inventory (SPIN), Social Interaction Anxiety Scale (SIAS), Social Phobia and Anxiety Inventory (SPAI), and Social Phobia Scale (SPS)
- Medical examination for differential diagnosis (if panic attacks are present and are not entirely situational): Screen for endocrine disorders, cardiovascular disease, respiratory disorders, temporal lobe epilepsy, vestibular disorders, and substance abuse (see "Secondary Causes of Anxiety").

Comments and Treatment Considerations

Initiate patient education regarding social phobia and discuss treatment options. SSRIs (sertraline, fluvoxamine, and paroxetine) are considered to be effective for treating social phobia. Other medications that are used for social phobia include SNRIs (venlafaxine), monoamine oxidase inhibitors (MAOIs) (phenelzine), benzodiazepines (clonazepam and alprazolam), and buspirone. The FDA has

advised monitoring patients for suicidal ideations after starting antidepressant medications.

Although β-adrenergic receptor antagonists (atenolol and propranolol) are sometimes effective for the associated performance anxiety, they are not considered to be effective for generalized social phobia. Cognitive-behavioral treatments, exposure-based treatments, applied relaxation, interpersonal psychotherapy (IPT), and social skills training have all shown some effectiveness as psychologic interventions for social phobia. CBT and exposure-based treatments appear most effective (and maintain effectiveness on posttreatment follow up studies).

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